Supporting Information

Regio- and Stereoselective Synthesis of (*E*)-Alkene *trans*-Xaa-Pro Dipeptide Mimetics Utilizing Organocopper-Mediated *Anti*-SN2' Reactions

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General Methods. All glassware and syringes were dried in an electric oven at 100°C prior to use. All melting points are uncorrected. Exact mass (HRMS) spectra were recorded on a JEOL JMS-01SG-2 or JMS-HX/HX 110A mass spectrometer. All NMR spectra were recorded in CDCl₃. Chemical shifts are reported in parts per million downfield from internal Me₄Si (s = singlet, d = doublet, dd double doublet, t = triplet, q = quadruplet, m = multiplet). Optical rotations were measured with a JASCO DIP-360 digital polarimeter. For flash chromatographies, silica gel 60H (silica gel for thin-layer chromatography, Merck) or silica gel 60 (finer than 230 mesh, Merck) was employed. Requisite 1-iodocyclopentene¹ and dimethyl-*N,N*-diisopropylphosphoramidite² were prepared according to literature. Protected amino acid derivatives **13** and **23**, were synthesized from L-serine using standard methodologies.³

- 1 Lee, K.; Wiemer, D. F. *Tetrahedron Lett.* **1993**, 34, 2433.
- 2 Bannwarth, W.; Trzeciak, A. *Helv. Chim. Acta* **1987**, 70, 175.
- 3 Bodanszky, M.; Bodanszky, A. *The Practice of Peptide Synthesis*, Springer-Verlag: Heidelberg, 1984.

(1*R*,2'*S*,*E*)-(tert-Butoxy)-*N*-{1-[(tert-butoxy)methyl]-2-[2'-

(hydroxymethyl)cyclopentylidene]ethyl}carboxamide (34) from 26.

By a procedure identical with that described for the synthesis of **28** from **25**, 1.6 g (5.0 mmol) of **26** was converted to 792 mg (47% yield) of *cis*-oxazolidinone **32** as colorless crystals. **32**: mp 89-92 °C; [α]_D²⁶ -5.7 (*c* = 1.59, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 5.86 (m, 1H), 5.08 (m, 1H), 4.28 (ddd, *J* = 7.1, 6.0, 2.1 Hz, 1H), 3.57 (dd, *J* = 9.2, 6.0 Hz, 1H), 3.32 (dd, *J* = 9.2, 2.1 Hz, 1H), 2.44-2.34 (m, 4H), 2.02-1.85 (m, 2H), 1.54 (s,

9H), 1.11 (s, 9H); Anal. Calcd for C₁₈H₂₉NO₅: C, 63.69; H, 8.61; N, 4.13. Found: C, 63.51; H, 8.43; N, 3.84.

Resulting oxazolidinone **32** (200 mg, 0.6 mmol) was subjected to reaction with the organocopper reagent (2.4 mmol) as described in the synthesis of **16** from **15**. After usual work-up, resulting crude materials including **33** was oxidized with KF (548 mg, 9.4 mmol) and 30% H₂O₂ solution (3.2 g, 28.3 mmol) at room temperature for 10 h. Usual work-up, followed by flash chromatographic purification, gave 126 mg (66% yield) of the title compound **34** as a colorless oil: $[\alpha]_D^{26} -15.0$ (c = 0.27, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 5.25 (ddd, *J* = 8.6, 4.4, 2.4 Hz, 1H), 4.97 (s, 1H), 4.17 (s, 1H), 3.62 (dd, *J* = 11.0, 5.8 Hz, 1H), 3.50 (dd, *J* = 11.0, 5.9 Hz, 1H), 3.40 (dd, *J* = 9.0, 4.2 Hz, 1H), 3.29 (dd, *J* = 9.0, 6.3 Hz, 1H), 2.58 (t, *J* = 5.5 Hz, 1H), 2.49-2.40 (m, 1H), 2.35-2.23 (m, 1H), 1.87-1.70 (m, 2H), 1.66-1.53 (m, 2H), 1.43 (s, 9H), 1.18 (s, 9H); HRMS (CI) *m/z* calcd for C₁₈H₃₄NO₄ (MH⁺) 328.2488, found 328.2477.

For assignment of the structure of **34**, *N*-Boc protected alcohol **34** was treated with TMSOTf (2 equiv.) and 2,6-lutidine (4 equiv.) in CH₂Cl₂ at 0 °C for 30 min to deprotect Boc group. The reaction was quenched with saturated NaHCO₃, extracted with EtOAc. The extract was subjected to the reaction with Mts-Cl and Et₃N in THF to obtained *N*-Mts protected alcohol **18**.

(1*S*,2'*R*,*E*)-2-{3'-(*tert*-Butoxy)-2'-[(*tert*-butoxy)carbonylamino]propylidene}cyclopentanecarboxylic acid (L-Ser-ψ(*E*)-CH=C]-D-Pro derivative 35) from 34.

By a procedure identical with that described for the synthesis of **20** from **18**, 127 mg (0.8 mmol) of **34** was converted to 84 mg (63% yield) of the title compound **35** as a colorless oil: $[\alpha]_D^{15} +18.2$ ($c = 0.71$, CHCl_3); ^1H NMR (270 MHz, CDCl_3) δ 5.50 (d, $J = 7.2$ Hz, 1H), 4.23 (s, 1H), 2.43-2.28 (m, 3H), 2.42-2.28 (m, 1H), 2.06-1.82 (m, 3H), 1.73-1.56 (m, 1H), 1.43 (s, 9H), 1.17 (s, 9H); HRMS (FAB) m/z calcd for $\text{C}_{18}\text{H}_{30}\text{NO}_5$ (MH^+) 340.2123, found 340.2120.

ORTEP diagram for 18

ORTEP diagram for 19

ORTEP diagram for DCHA salt of 31

CC(C)(C)OC[C@H](NC(=O)C1CCC1)C=C[C@@H](O)C1CCCC1

ORTEP diagram for 37b

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 SF02: 300.133
 SF2: 300.133
 SY: 210.030000
 Q1: 5450.000
 Q2: 6535
 Q3: 6535
 Q4: 6535
 Q5: 6535
 SW: 6024.096
 SM2: 6024.096
 HZ/PT: 0.184
 VD: 0.0
 PW: 4.5
 RD: 5.560
 AQ: 5.439
 RB: 40
 RE: 237
 TE: 237
 DE: 106.3
 DR: 12
 DM: 12
 FM: 7600
 O2: 0.0
 DP: 15L P0
 LB: 0.0
 GB: 0.0
 NC: 4
 CX: 33.00
 CY: 0.0
 F1: 8.000P
 MI: 0.01
 DC: 1.000
 HZ/CM: 74.578
 PPM/CM: 5.248
 SR: 3367.08

FK - A50

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 SF0 300.130
 SF02 250.130
 SF2 300.133
 SF2 300.130
 O1 210.000
 O1 5450.000
 S1 65536
 ID 65536
 SM 6034.096
 SZ 6034.184
 WZ/P1 0.0
 VD 0.0
 PW 4.5
 AQ 5.360
 RG 32.439
 NS 32
 TE 297
 DE 105.3
 DR 12
 DW 83
 FM 7600
 O2 0.0
 DP 15L P0
 LB 0.0
 GB 0.0
 AC 4
 CX 30.0
 CX 0.0
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 F2 -.200P
 MI 1.01
 UC/CM 1.500
 PR/CM 74.248
 IS 5.248
 SR 3367.27

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 AQ 2.647004 sec
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 DW 40.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec
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 GB 0
 CB 0
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S1	65536
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S2	502.986
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AQ	5.439
RQ	32
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DE	106.3
DR	12
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OZ	0.0
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LB	0.0
NC	0.0
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CY	33.00
CP	0.00P
F	-200P
M1	.01
DM	1.000
PC	74.248
TS	3385.61

22-MAY-01 15:30:58

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OBNUC 1H

EXMOD NON

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112.00 kHz

5800.0 Hz

32768

POINT

FREQU 5405.4 Hz

SCANS 16

3.031 sec

ACQTM

PD 3.969 sec

PW1 5.1 us

IRNUC 1H

CTEMP 19.6 c

SLVNT CDCL3

EXREF 0.00 ppm

BF 0.16 Hz

RGAIN 19

OPERATOR :

PK-G36

Current Data Parameters
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 PROCNO 1

F2 - Acquisition Parameters
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 Time 12.05
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 PROBD 5 mm TXI 1H-
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
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 DS 2
 SWH 12376.237 Hz
 FIDRES 0.188846 Hz
 AQ 2.6477844 sec
 RG 395
 RW 40.400 usec
 DE 6.00 usec
 TE 300.0 K
 DI 1.00000000 sec

===== CHANNEL f1 =====
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 P1 10.70 usec
 PL1 0.00 dB
 SFO1 600.1337060 MHz

F2 - Processing parameters
 SI 32768
 SF 600.1300141 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
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 F1 4801.04 Hz
 F2P -120.0 ppm
 F2 -120.0 Hz
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 HZCM 164.03554 Hz/cm

17-JAN-02 09:51:07
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 OBSET 112.00 kHz
 OFBIN 5800.0 Hz
 POINT 32768
 FREQ 5405.4 Hz
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 ACQIM 3.031 sec
 PD 3.969 sec
 PM 5.1 us
 TRNUC 1H
 CTEMP 22.2 c
 SLVNT CDCL3
 EXREF 0.0 ppm
 BF 0.16 Hz
 RGAIN 18
 OPERATOR

14-MAR-02 15.07.31
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 EXMOD NON
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 112.00 MHz
 5800 -1
 32768
 5405.4 Hz
 16
 3 023 000
 2 949 000
 5.1 00
 PM1
 IR UC 1H
 CTETP 21.7 C
 SLVNT CDCL2
 EXREF
 0.00 DI^m
 0.10 Hz
 RGA N 12
 OPER TOR